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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,927	01/22/2004	Cun Zhuang	MPIP:101US	5744

24041 7590 06/15/2006

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 06/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/762,927	ZHUANG ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/4/04, 5/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT OF IDS, STATUS OF THE APPLICATION AND CLAIMS

1. The information disclosure statement (IDS) and Form PTO-1449 filed 05/04/04 and 05/07/04, respectively are acknowledged, entered and considered. Claims 1-37 are now pending in the application.

CLAIM REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 and 13-14 are indefinite in the recitation "a molecular weight equal to or greater than 14,000" (claims 1-4 and 13) and "a molecular weight of 20,000" (claims 5 and 14) because the claims fail to identify whether the units of molecular weights are Dalton or kilo Dalton. Appropriate clarification is required.

Claims 25, 35 and 37 are indefinite and confusing in the recitation "functional food product" because the phrase is not defined in the specification or in the claims and it is not understood what kind of food product the phrase is intended to encompass. Appropriate clarification is required.

The syntax of claim 25 is indefinite and vague in the recitation "A health food or functional food product which may claim antidiabetic, antihypertensive, antiobesity and antihyperlipidemic activities..." because it is not clear what the claim is intended to claim. Appropriate clarification is required.

CLAIMS REJECTION-35 U.S.C. § 102(b)

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4, 6, 9, 10 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Nanba et al (U.S. Patent No. 5,854,404).

The prior art of Nanba et al ('404 patent) discloses like the instantly claimed invention methods for preparing bioactive glycoprotein by the steps of thermally extracting Mycelia or fruit bodies of *Grifola frondosa* with water at 50^0 to 135^0 C, adding alcohol such as ethanol to the resulting water-soluble extract at a final concentration of 20 to 60% volume (low concentration addition), allowing to stand at a temperature of 1^0 to 25^0 C for 1-20 hours for floating to occur, and removing floating matter on the liquid or in the liquid or adhering matter to the vessel wall, and these are removed by filtration or with a pipette, net, etc. (filtration encompasses ultrafiltration, centrifugal filtration, gel filtration chromatography, etc.). See e.g., cols. 1 and 2, claims 1-4 and 15-16 as

directed to claims 1, 3, 4, 6, 9, 10 and 12. It is noted that the molecular weight of the fraction collected from the supernatant is equal or greater than 14,000 as claimed in claim 1, however, the '404 patent discloses on col. 3, lines 9-11 that based on gel filtration chromatography, the molecular weight is distributed around 1,000,000. Thus, since greater than 14,000 would encompass and would not exclude the molecular weight of the prior art, and as such, the claimed molecular weight would read on the prior art molecular weight. Therefore, the '404 patent clearly discloses a method for preparing a bioactive glycoprotein by extracting and fractionating Mycelia or fruit bodies of "Maitake" mushroom (Grifola) at the conditions/situations recited in the claims, and as such, substantially discloses the invention as claimed and anticipates claims 1, 3, 4, 6, 9, 10 and 12 as drafted.

CLAIMS REJECTION-35 U.S.C. § 103(a)

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nanba et al (U.S. Patent No. 5,854,404) taken with Kubo et al (Biol. Pharm. Bull. Vol. 17, No. 8, pages 1106-1110, 1994).

Nanba et al ('404 patent) as discussed above discloses like the instantly claimed invention methods for preparing bioactive glycoprotein by the steps of thermally extracting Mycelia or fruit bodies of *Grifola frondosa* with water at 50^0 to 135^0 C, adding alcohol such as ethanol to the resulting water-soluble extract at a final concentration of 20 to 60% volume (low concentration addition), allowing to stand at a temperature of 1^0 to 25^0 C for 1-20 hours for floating to occur, and removing floating matter on the liquid or in the liquid or adhering matter to the vessel wall, and these are removed by filtration or with a pipette, net, etc. (filtration encompasses ultrafiltration, centrifugal filtration, gel filtration chromatography, etc.). See e.g., cols. 1 and 2, claims 1-4 and 15-16 as directed to claims 1, 3, 4, 6, 9, 10 and 12. It is noted that the molecular weight of the fraction collected from the supernatant is equal or greater than 14,000 as claimed in claim 1, however, the '404 patent discloses on col. 3, lines 9-11 that based on gel filtration chromatography, the molecular weight is distributed around 1,000,000. Thus, since greater than 14,000 would encompass and would not exclude the molecular

weight of the prior art, and as such, the claimed molecular weight would read on the prior art molecular weight. Therefore, the '404 patent clearly discloses a method for preparing a bioactive glycoprotein by extracting and fractionating Mycelia or fruit bodies of "Maitake" mushroom (Grifola) at the conditions/situations recited in the claims.

The '404 patent on col. 4, lines 34 to 38 states that the substances obtained according to the present invention is of low toxicity and high safety and can be orally administered as health foods (encompass food additive) and pharmaceutical preparations, especially antitumor agent, in the form of tablets, capsules, liquid, syrup, etc. Further, methods of manufacturing all the above configurations are known to those skilled in the art as acknowledged on page 10, lines 1 and 2 in the instant specification. Thus, in view of the above, and in view of the primary reference's teachings, one of ordinary skill in the art would easily formulate the bioactive glycoprotein product in the desired form, and as such meet the limitations of claims 21-24 and 30-33.

With respect to the atmospheric pressure recited in claim 8, the '404 patent similarly performs hot water extraction at about the same temperature i.e., about 120^0 C and at 2 atmospheric pressure (See e.g., col. 2, lines 6-10), and as such, meets the limitation of claim 8.

The primary reference of Nanba et al. differs from claims 1-37 in not teaching health food product comprising a bioactive glycoprotein having the properties of antidiabetic, antihypertensive, antiobesity and antihyperlipidemic activities and a glycoprotein having a protein to saccharide ratio from about 75:25 to about 90:10 and an average molecular weight of about 20,000. Although, the inventors in the primary

reference of '404 patent (i.e., Hiroaki Nanba and Keiko Kubo) as discussed above have shown that a glucan obtained from maitake (*Grifola frondosa*), posses antitumor activity; however, the secondary reference of Kubo et al (i.e., two of the three authors, namely Keiko Kubo and Hiroaki Nanba are inventors of the primary reference of '404 patent) have confirmed that the fruit body of *Grifola frondosa* (maitake), *Basidiomycetes* to contain substances with antidiabetic activity. When 1 g/d of powdered fruit body of maitake was given orally to a genetically diabetic mouse (KK-A^y), blood glucose reduction was observed, in contrast to the control group in which the blood glucose increased with ageing. Moreover, levels of insulin and triglyceride in plasma demonstrated a change similar to blood glucose with feeding of maitake. Ether-ethanol-soluble (ES) and hot water-soluble (WS) fractions were prepared from fruit body and their hypoglycemic activity was examined. Blood glucose-lowering activity was found when ES-fraction or WS-50% ethanol float (X) fraction was administered orally, but other WS-fractions were inactive. These results suggest that the antidiabetic activity was present not only in the ES-fraction consisting of lipid but also in the X-fraction of peptidoglycan (sugar: protein = 65:35). See e.g., abstract. Further, the secondary reference on page 1109 under Discussion states that fruit bodies of maitake inhibit the weight increase even in mice, which have the obesity gene. Levels of blood glucose, plasma insulin and triglyceride in M-feed mice were all lower with significance of differences compared of the control groups. The secondary reference concludes by stating that further work to isolate the active agent and elucidate its function and mechanism are now in progress. Thus, the secondary

reference has clearly shown the extraction of health food product from *Grifola frondosa* comprising a bioactive glycoprotein having the properties of antidiabetic, antihypertensive, antiobesity and antihyperlipidemic activities.

Therefore, in view of the secondary reference's teachings, one of ordinary skill in the art at the time the invention was made would have been motivated to apply the teachings of the secondary reference (i.e., use of a bioactive glycoprotein product for antidiabetic, antihypertensive, antiobesity and antihyperlipidemic activities) to the primary reference's teachings of a bioactive glycoprotein product for use in antitumor activity since both use the same bioactive glycoprotein product as taught by the secondary reference because such features are known or suggested in the art, as seen in the secondary reference, and including such features into the method and/or use of the primary reference would have been obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages thereof.

With respect to the ratio of a protein to saccharide ranging from about 75:25 to about 90:10 as recited in claims 13 and 14, the secondary reference cites the ratio of sugar: protein = 65:35, while the primary reference states on col. 2, lines 48-57 that analysis of the substance obtained by the present invention is a glucan/protein complex where the glucan/protein ratio varies mainly in the range of 80:20 to 99:1 depending on the qualities of Grifola as the starting material, conditions for extraction and purification, etc. Thus clearly suggesting that it is within the skill of the art to which this invention pertains to adjust the ratio of glucan/protein based on the conditions discussed above.

In regard to the molecular weight equal to or greater than 14,000 and an average molecular weight of about 20,000, the molecular weights are not disclosed in the primary reference as claimed; however, the claims do not define the molecular weights as functional limitations, rather, the claims define the molecular weights as property of a bioactive glycoprotein. Further, the primary reference of '404 patent as well as the claimed invention has substantially the same compound/formulation (i.e., a bioactive glycoprotein extracted from the fruiting body of *Grifola frondosa*). Thus, the bioactive glycoprotein extracted and fractionated from the fruiting body of *Grifola frondosa* solution of the primary reference would have the same molecular weights as claimed because the molecular weight is an expected property, which is a characteristic when a solution is purified from the same compound/formulation.

With respect to the claimed compound/formulation further comprising vitamins, minerals, herbs, mushrooms, and other nutritional ingredients. Use of such food additives in a health food product are known in the art and it is within the skill of this invention for one of ordinary skill in the art to formulate the claimed compound/formulation by supplementing a variety of dietary products such as vitamins, minerals, herbs, mushrooms, and other nutritional ingredients for the intended purposes of using as an additive for health foods having the properties of antidiabetic, antihypertensive, antiobesity and antihyperlipidemic activities. Thus, in view of the above, the addition of vitamins, minerals herbs, mushrooms and other nutritional ingredients appears to be obvious as taught by the teachings of the prior art and what is conventional and routine in the art at the time the invention was made

because one of ordinary skill in the art would have been motivated to modify the process taught by the prior art by including an additional components and/or ingredients (i.e., vitamins, minerals, herbs, mushrooms and other nutritional ingredients) which are conventional and known in the art, since it is not unobvious to combine two or more ingredients or components or compositions which are conventional and known in the art to be useful for the same purposes. See *In re Kerhoven*, 205 USPQ 1069 (CCPA 1980).

Therefore, in view of the above and in view of the combined teachings of the prior art at the time the invention was made, one of ordinary skill in the art would have been motivated to employ methods for preparing a bioactive glycoprotein by extracting the fruiting body of *Grifola frondosa* (maitake) at the conditions/situations recited in the claims and products thereof having properties of antidiabetic, antihypertensive, antiobesity and antihyperlipidemic activities and effects, absent of sufficient objective factual evidence or unexpected results to the contrary.

CITATION OF RELEVANT PRIOR ART

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Kusano et al (Biosc. Biotechnol. Biochem. Vol. 65, No. 1, pages 109-114, 2001) investigate the isolation and purification of the antidiabetic component from white-skinned sweet potato (WSSP).

CONCLUSION AND FUTURE CORRESPONDANCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on (571) 272 0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JON WEBER
SUPERVISORY PATENT EXAMINER

Mohamed/AAM
June 9, 2006